SEQUENCE LISTING

<110> Bayer Corporation

<120> Protein Having Activity As An Angiogenesis Modulator

<130> MSB-7265-PCT

<140> PCT/US 01/10222
<141> 2001-03-30

<150> US 60/266,300
<151> 2000-03-31

<160> 34

<170> PatentIn version 3.1

<210> 1
<211> 208
<212> PRT
<213> Homo sapiens

<400> 1

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Gln Val His Gly Gly Phe Ser Gln Trp Ser Ala Trp Arg Ala Cys Ser
1               5                   10                  15


Val Thr Cys Gly Lys Gly Ile Gln Lys Arg Ser Arg Leu Cys Asn Gln
            20                  25                  30


Pro Leu Pro Ala Asn Gly Gly Lys Pro Cys Gln Gly Ser Asp Leu Glu
        35                  40                  45


Met Arg Asn Cys Gln Asn Lys Pro Cys Pro Val Asp Gly Ser Trp Ser
    50                  55                  60


Glu Trp Ser Leu Trp Glu Glu Cys Thr Arg Ser Cys Gly Arg Gly Asn
65                  70                  75                  80


Gln Thr Arg Thr Arg Thr Cys Asn Asn Pro Ser Val Gln His Gly Gly
                85                  90                  95


Arg Pro Cys Glu Gly Asn Ala Val Glu Ile Ile Met Cys Asn Ile Arg
            100                 105                 110


Pro Cys Pro Val His Gly Ala Trp Ser Ala Trp Gln Pro Trp Gly Thr
        115                 120                 125
```

```
Cys Ser Glu Ser Cys Gly Lys Gly Thr Gln Thr Arg Ala Arg Leu Cys
    130                 135                 140

Asn Asn Pro Pro Pro Ala Phe Gly Gly Ser Tyr Cys Asp Gly Ala Glu
145                 150                 155                 160

Thr Gln Met Gln Val Cys Asn Glu Arg Asn Cys Pro Ile His Gly Lys
                165                 170                 175

Trp Ala Thr Trp Ala Ser Trp Ser Ala Cys Ser Val Ser Cys Gly Gly
            180                 185                 190

Gly Ala Arg Gln Arg Thr Arg Gly Cys Ser Asp Pro Val Pro Gln Tyr
        195                 200                 205
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<210> 2
<211> 51
<212> PRT
<213> Artificial Sequence

<220>
<223> Random sequence

<400> 2

```
Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Ala Asn Pro Gln Leu
1               5                   10                  15

Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu
            20                  25                  30

Arg Asp Asn Gln Leu Val Val Glu Gly Leu Tyr Leu Ile Tyr Ser Gln
        35                  40                  45

Val Leu Phe
    50
```

<210> 3
<211> 52
<212> PRT
<213> Artificial Sequence

<220>
<223> Random sequence

<400> 3

```
Arg Ala Pro Phe Lys Lys Ser Trp Ala Tyr Leu Gln Val Ala Lys His
```

1 5 10 15

Lys Leu Ser Trp Asn Lys Asp Gly Ile Leu His Gly Val Arg Tyr Gln
20 25 30

Asp Gly Asn Leu Val Ile Gln Phe Pro Gly Leu Tyr Phe Ile Ile Cys
35 40 45

Gln Leu Gln Phe
50

<210> 4
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> FLAG sequence for expressed protein

<400> 4

Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

<210> 5
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Sequence with antineoangiogenic activity

<400> 5

Cys Ser Val Thr Cys Gly
1 5

<210> 6
<211> 50
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 6

Asp Gly Trp Ser Pro Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys
1 5 10 15

Gly Asn Gly Ile Gln Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn
20 25 30

Arg Cys Glu Gly Ser Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu
35 40 45

Cys Asp
50

<210> 7
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 7

Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser Val Thr Cys
1 5 10 15

Gly Asp Gly Val Ile Thr Arg Ile Arg Leu Cys Asn Ser Pro Ser Pro
20 25 30

Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu Thr Lys Ala
35 40 45

Cys Lys Lys Asp Ala Cys Pro
50 55

<210> 8
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 8

Gly Gly Trp Gly Pro Trp Ser Pro Trp Asp Ile Cys Ser Val Thr Cys
1 5 10 15

Gly Gly Gly Val Gln Lys Arg Ser Arg Leu Cys Asn Asn Pro Thr Pro
20 25 30

Gln Phe Gly Gly Lys Asp Cys Val Gly Asp Val Thr Glu Asn Gln Ile

35 40 45

Cys Asn Lys Gln Asp Cys Pro
50 55

<210> 9
<211> 50
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 9

Glu Gly Trp Ser Pro Trp Ala Glu Trp Thr Gln Cys Ser Val Thr Cys
1 5 10 15

Gly Ser Gly Thr Gln Gln Arg Gly Arg Ser Cys Asp Val Thr Ser Asn
20 25 30

Thr Cys Leu Gly Pro Ser Ile Gln Thr Arg Ala Cys Ser Leu Ser Lys
35 40 45

Cys Asp
50

<210> 10
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 10

Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser Val Thr Cys
1 5 10 15

Gly Val Gly Asn Ile Thr Arg Ile Arg Leu Cys Asn Ser Pro Val Pro
20 25 30

Gln Met Gly Gly Lys Asn Cys Lys Gly Ser Gly Arg Glu Thr Lys Ala
35 40 45

Cys Gln Gly Ala Pro Cys Pro
50 55

<210> 11
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin sequence

<400> 11

Gly Arg Trp Ser Pro Trp Ser Pro Trp Ser Ala Cys Thr Val Thr Cys
1 5 10 15

Ala Gly Gly Ile Arg Glu Arg Thr Arg Val Cys Asn Ser Pro Glu Pro
20 25 30

Gln Tyr Gly Gly Lys Ala Cys Val Gly Asp Val Gln Glu Arg Gln Met
35 40 45

Cys Asn Lys Arg Ser Cys Pro
50 55

<210> 12
<211> 54
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 12

Gly Gly Trp Lys Leu Trp Ser Leu Trp Gly Glu Cys Thr Arg Asp Cys
1 5 10 15

Gly Gly Gly Leu Gln Thr Arg Thr Arg Thr Cys Leu Pro Ala Pro Gly
20 25 30

Val Glu Gly Gly Gly Cys Glu Gly Val Leu Glu Glu Gly Arg Gln Cys
35 40 45

Asn Arg Glu Ala Cys Gly
50

<210> 13
<211> 53
<212> PRT

<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 13

Pro Ala Ala Glu Glu Trp Ser Pro Trp Ser Val Cys Ser Ser Thr Cys
1 5 10 15

Gly Glu Gly Trp Gln Thr Arg Thr Arg Phe Cys Val Ser Ser Ser Tyr
20 25 30

Ser Thr Gln Cys Ser Gly Pro Leu Arg Glu Gln Arg Leu Cys Asn Asn
35 40 45

Ser Ala Val Cys Pro
50

<210> 14
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 14

Gly Ala Trp Asp Glu Trp Ser Pro Trp Ser Leu Cys Ser Ser Thr Cys
1 5 10 15

Gly Arg Gly Phe Arg Asp Arg Thr Arg Thr Cys Arg Pro Pro Gln Phe
20 25 30

Gly Gly Asn Pro Cys Glu Gly Pro Glu Lys Gln Thr Lys Phe Cys Asn
35 40 45

Ile Ala Leu Cys Pro
50

<210> 15
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 15

Gly Asn Trp Asn Glu Trp Ser Ser Trp Ser Ala Cys Ser Ala Ser Cys
1 5 10 15

Ser Gln Gly Arg Gln Gln Arg Thr Arg Glu Cys Asn Gly Pro Ser Tyr
20 25 30

Gly Gly Ala Glu Cys Gln Gly His Trp Val Glu Thr Arg Asp Cys Phe
35 40 45

Leu Gln Gln Cys Pro
50

<210> 16
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 16

Gly Lys Trp Gln Ala Trp Ala Ser Trp Gly Ser Cys Ser Val Thr Cys
1 5 10 15

Gly Ala Gly Ser Gln Arg Arg Glu Arg Val Cys Ser Gly Pro Phe Phe
20 25 30

Gly Gly Ala Ala Cys Gln Gly Pro Gln Asp Glu Tyr Arg Gln Cys Gly
35 40 45

Thr Gln Arg Cys Pro
50

<210> 17
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 17

Pro Ala Ala Glu Glu Trp Ser Pro Trp Ser Val Cys Ser Leu Thr Cys
1 5 10 15

Gly Gln Gly Leu Gln Val Arg Thr Arg Ser Cys Val Ser Ser Pro Tyr
20 25 30

Gly Thr Leu Cys Ser Gly Pro Leu Arg Glu Thr Arg Pro Cys Asn Asn
35 40 45

Ser Ala Thr Cys Pro
50

<210> 18
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 18

Gly Val Trp Glu Glu Trp Gly Ser Trp Ser Leu Cys Ser Arg Ser Cys
1 5 10 15

Gly Arg Gly Ser Arg Ser Arg Met Arg Thr Cys Val Pro Pro Gln His
20 25 30

Gly Gly Lys Ala Cys Glu Gly Pro Glu Leu Gln Thr Lys Leu Cys Ser
35 40 45

Met Ala Ala Cys Pro
50

<210> 19
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 19

Gly Gln Trp Leu Glu Trp Gly Pro Trp Gly Pro Cys Ser Thr Ser Cys
1 5 10 15

Ala Asn Gly Thr Gln Gln Arg Ser Arg Lys Cys Ser Val Ala Gly Pro
20 25 30

Ala Trp Ala Thr Cys Thr Gly Ala Leu Thr Asp Thr Arg Glu Cys Ser
35 40 45

Asn Leu Glu Cys Pro
50

<210> 20
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 20

Ser Lys Trp Gly Pro Trp Asn Ala Trp Ser Leu Cys Ser Lys Thr Cys
1 5 10 15

Asp Thr Gly Trp Gln Arg Arg Phe Arg Met Cys Gln Ala Thr Gly Thr
20 25 30

Gln Gly Tyr Pro Cys Glu Gly Thr Gly Glu Glu Val Lys Pro Cys Ser
35 40 45

Glu Lys Arg Cys Pro
50

<210> 21
<211> 52
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 21

Ser Gly Val Glu Glu Trp Ser Gln Trp Ser Thr Cys Ser Val Thr Cys
1 5 10 15

Gly Gln Gly Ser Gln Val Arg Thr Arg Thr Cys Val Ser Pro Tyr Gly
20 25 30

Thr His Cys Ser Gly Pro Leu Arg Glu Ser Arg Val Cys Asn Asn Thr
35 40 45

Ala Leu Cys Pro

50

<210> 22
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 22

Gly Val Trp Glu Glu Trp Ser Pro Trp Ser Leu Cys Ser Phe Thr Cys
1 5 10 15

Gly Arg Gly Gln Arg Thr Arg Thr Arg Ser Cys Thr Pro Pro Gln Tyr
20 25 30

Gly Gly Arg Pro Cys Glu Gly Pro Glu Thr His His Lys Pro Cys Asn
35 40 45

Ile Ala Leu Cys Pro
50

<210> 23
<211> 53
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 23

Gly Gln Trp Gln Glu Trp Ser Ser Trp Ser Gln Cys Ser Val Thr Cys
1 5 10 15

Ser Asn Gly Thr Gln Gln Arg Ser Arg Gln Cys Thr Ala Ala Ala His
20 25 30

Gly Gly Ser Glu Cys Arg Gly Pro Trp Ala Glu Ser Arg Glu Cys Tyr
35 40 45

Asn Pro Glu Cys Thr
50

<210> 24
<211> 53

<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 24

Gly Gln Trp Asn Gln Trp Gly His Trp Ser Gly Cys Ser Lys Ser Cys
1 5 10 15

Asp Gly Gly Trp Glu Arg Arg Ile Arg Thr Cys Gln Gly Ala Val Ile
20 25 30

Thr Gly Gln Gln Cys Glu Gly Thr Gly Glu Glu Val Arg Arg Cys Ser
35 40 45

Glu Gln Arg Cys Pro
50

<210> 25
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 25

Gly Gly Phe Ser Gln Trp Ser Ala Trp Arg Ala Cys Ser Val Thr Cys
1 5 10 15

Gly Lys Gly Ile Gln Lys Arg Ser Arg Leu Cys Asn Gln Pro Leu Pro
20 25 30

Ala Asn Gly Gly Lys Pro Cys Gln Gly Ser Asp Leu Glu Met Arg Asn
35 40 45

Cys Gln Asn Lys Pro Cys Pro
50 55

<210> 26
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 26

Gly Ser Trp Ser Glu Trp Ser Leu Trp Glu Glu Cys Thr Arg Ser Cys
1 5 10 15

Gly Arg Gly Asn Gln Thr Arg Thr Arg Thr Cys Asn Asn Pro Ser Val
20 25 30

Gln His Gly Gly Arg Pro Cys Glu Gly Asn Ala Val Glu Ile Ile Met
35 40 45

Cys Asn Ile Arg Pro Cys Pro
50 55

<210> 27
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 27

Gly Ala Trp Ser Ala Trp Gln Pro Trp Gly Thr Cys Ser Glu Ser Cys
1 5 10 15

Gly Lys Gly Thr Gln Thr Arg Ala Arg Leu Cys Asn Asn Pro Pro Pro
20 25 30

Ala Phe Gly Gly Ser Tyr Cys Asp Gly Ala Glu Thr Gln Met Gln Val
35 40 45

Cys Asn Glu Arg Asn Cys Pro
50 55

<210> 28
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 28

Gly Lys Trp Ala Thr Trp Ala Ser Trp Ser Ala Cys Ser Val Ser Cys
1 5 10 15

Gly Gly Gly Ala Arg Gln Arg Thr Arg Gly Cys Ser Asp Pro Val Pro
20 25 30

Gln Tyr Gly Gly Arg Lys Cys Glu Gly Ser Asp Val Gln Ser Asp Phe
35 40 45

Cys Asn Ser Asp Pro Cys Pro
50 55

<210> 29
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 29

Gly Asn Trp Ser Pro Trp Ser Gly Trp Gly Thr Cys Ser Arg Thr Cys
1 5 10 15

Asn Gly Gly Gln Met Arg Arg Tyr Arg Thr Cys Asp Asn Pro Pro Pro
20 25 30

Ser Asn Gly Gly Arg Ala Cys Gly Gly Pro Asp Ser Gln Ile Gln Arg
35 40 45

Cys Asn Thr Asp Met Cys Pro
50 55

<210> 30
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Isolated type 1 thrombospondin domain sequence

<400> 30

Gly Ser Trp Gly Ser Trp His Ser Trp Ser Gln Cys Ser Ala Ser Cys
1 5 10 15

Gly Gly Gly Glu Lys Thr Arg Lys Arg Leu Cys Asp His Pro Val Pro
20 25 30

```
Val Lys Gly Gly Arg Pro Cys Pro Gly Asp Thr Thr Gln Val Thr Arg
        35                  40                  45

Cys Asn Val Gln Ala Cys Pro
    50                  55
```

<210> 31
<211> 197
<212> PRT
<213> Homo sapiens

<400> 31

```
Gln Trp Ser Ala Trp Arg Ala Cys Ser Val Thr Cys Gly Lys Gly Ile
1               5                   10                  15

Gln Lys Arg Ser Arg Leu Cys Asn Gln Pro Leu Pro Ala Asn Gly Gly
            20                  25                  30

Lys Pro Cys Gln Gly Ser Asp Leu Glu Met Arg Asn Cys Gln Asn Lys
        35                  40                  45

Pro Cys Pro Val Asp Gly Ser Trp Ser Glu Trp Ser Leu Trp Glu Glu
    50                  55                  60

Cys Thr Arg Ser Cys Gly Arg Gly Asn Gln Thr Arg Thr Arg Thr Cys
65                  70                  75                  80

Asn Asn Pro Ser Val Gln His Gly Gly Arg Pro Cys Glu Gly Asn Ala
                85                  90                  95

Val Glu Ile Ile Met Cys Asn Ile Arg Pro Cys Pro Val His Gly Ala
            100                 105                 110

Trp Ser Ala Trp Gln Pro Trp Gly Thr Cys Ser Glu Ser Cys Gly Lys
        115                 120                 125

Gly Thr Gln Thr Arg Ala Arg Leu Cys Asn Asn Pro Pro Pro Ala Phe
    130                 135                 140

Gly Gly Ser Tyr Cys Asp Gly Ala Glu Thr Gln Met Gln Val Cys Asn
145                 150                 155                 160

Glu Arg Asn Cys Pro Ile His Gly Lys Trp Ala Thr Trp Ala Ser Trp
```

165 170 175

Ser Ala Cys Ser Val Ser Cys Gly Gly Gly Ala Arg Gln Arg Thr Arg
180 185 190

Gly Cys Ser Asp Pro
195

<210> 32
<211> 194
<212> PRT
<213> Homo sapiens

<400> 32

Glu Trp Ser Pro Trp Ser Val Cys Ser Ser Thr Cys Gly Glu Gly Trp
1 5 10 15

Gln Thr Arg Thr Arg Phe Cys Val Ser Ser Ser Tyr Ser Thr Gln Cys
20 25 30

Ser Gly Pro Leu Arg Glu Gln Arg Leu Cys Asn Asn Ser Ala Val Cys
35 40 45

Pro Val His Gly Ala Trp Asp Glu Trp Ser Pro Trp Ser Leu Cys Ser
50 55 60

Ser Thr Cys Gly Arg Gly Phe Arg Asp Arg Thr Arg Thr Cys Arg Pro
65 70 75 80

Pro Gln Phe Gly Gly Asn Pro Cys Glu Gly Pro Glu Lys Gln Thr Lys
85 90 95

Phe Cys Asn Ile Ala Leu Cys Pro Gly Arg Ala Val Asp Gly Asn Trp
100 105 110

Asn Glu Trp Ser Ser Trp Ser Ala Cys Ser Ala Ser Cys Ser Gln Gly
115 120 125

Arg Gln Gln Arg Thr Arg Glu Cys Asn Gly Pro Ser Tyr Gly Gly Ala
130 135 140

Glu Cys Gln Gly His Trp Val Glu Thr Arg Asp Cys Phe Leu Gln Gln
145 150 155 160

```
Cys Pro Val Asp Gly Lys Trp Gln Ala Trp Ala Ser Trp Gly Ser Cys
                165                 170                 175

Ser Val Thr Cys Gly Ala Gly Ser Gln Arg Arg Glu Arg Val Cys Ser
            180                 185                 190

Gly Pro
```

<210> 33
<211> 1336
<212> PRT
<213> Homo sapiens

<400> 33

```
Thr Pro Ile Gly Arg Pro Arg Ile Arg His Gln Asp Lys Arg Thr Val
1               5                   10                  15

Asp Leu Thr Val Gln Val Pro Pro Ser Ile Ala Asp Glu Pro Thr Asp
            20                  25                  30

Phe Leu Val Thr Lys His Ala Pro Ala Val Ile Thr Cys Thr Ala Ser
        35                  40                  45

Gly Val Pro Phe Pro Ser Ile His Trp Thr Lys Asn Gly Ile Arg Leu
    50                  55                  60

Leu Pro Arg Gly Asp Gly Tyr Arg Ile Leu Ser Ser Gly Ala Ile Glu
65                  70                  75                  80

Ile Leu Ala Thr Gln Leu Asn His Ala Gly Arg Tyr Thr Cys Val Ala
                85                  90                  95

Arg Asn Ala Ala Gly Ser Ala His Arg His Val Thr Leu His Val His
            100                 105                 110

Glu Pro Pro Val Ile Gln Pro Gln Pro Ser Glu Leu His Val Ile Leu
        115                 120                 125

Asn Asn Pro Ile Leu Leu Pro Cys Glu Ala Thr Gly Thr Pro Ser Pro
    130                 135                 140

Phe Ile Thr Trp Gln Lys Glu Gly Ile Asn Val Asn Thr Ser Gly Arg
```

```
145                 150                 155                 160

Asn His Ala Val Leu Pro Ser Gly Gly Leu Gln Ile Ser Arg Ala Val
                165                 170                 175

Arg Glu Asp Ala Gly Thr Tyr Met Cys Val Ala Gln Asn Pro Ala Gly
            180                 185                 190

Thr Ala Leu Gly Lys Ile Lys Leu Asn Val Gln Val Pro Pro Val Ile
        195                 200                 205

Ser Pro His Leu Lys Glu Tyr Val Ile Ala Val Asp Lys Pro Ile Thr
    210                 215                 220

Leu Ser Cys Glu Ala Asp Gly Leu Pro Pro Pro Asp Ile Thr Trp His
225                 230                 235                 240

Lys Asp Gly Arg Ala Ile Val Glu Ser Ile Arg Gln Arg Val Leu Ser
                245                 250                 255

Ser Gly Ser Leu Gln Ile Ala Phe Val Gln Pro Gly Asp Ala Gly His
            260                 265                 270

Tyr Thr Cys Met Ala Ala Asn Val Ala Gly Ser Ser Ser Thr Ser Thr
        275                 280                 285

Lys Leu Thr Val His Val Pro Pro Arg Ile Arg Ser Thr Lys Gly His
    290                 295                 300

Tyr Thr Val Asn Glu Asn Ser Gln Ala Ile Leu Pro Cys Val Ala Asp
305                 310                 315                 320

Gly Ile Pro Thr Pro Ala Ile Asn Trp Lys Lys Asp Asn Val Leu Leu
                325                 330                 335

Ala Asn Leu Leu Gly Lys Tyr Thr Ala Glu Pro Tyr Gly Glu Leu Ile
            340                 345                 350

Leu Glu Asn Val Val Leu Glu Asp Ser Gly Phe Tyr Thr Cys Val Ala
        355                 360                 365

Asn Asn Ala Ala Gly Glu Asp Thr His Thr Val Ser Leu Thr Val His
    370                 375                 380
```

```
Val Leu Pro Thr Phe Thr Glu Leu Pro Gly Asp Val Ser Leu Asn Lys
385                 390                 395                 400

Gly Glu Gln Leu Arg Leu Ser Cys Lys Ala Thr Gly Ile Pro Leu Pro
                405                 410                 415

Lys Leu Thr Trp Thr Phe Asn Asn Asn Ile Ile Pro Ala His Phe Asp
            420                 425                 430

Ser Val Asn Gly His Ser Glu Leu Val Ile Glu Arg Val Ser Lys Glu
        435                 440                 445

Asp Ser Gly Thr Tyr Val Cys Thr Ala Glu Asn Ser Val Gly Phe Val
    450                 455                 460

Lys Ala Ile Gly Phe Val Tyr Val Lys Glu Pro Pro Val Phe Lys Gly
465                 470                 475                 480

Asp Tyr Pro Ser Asn Trp Ile Glu Pro Leu Gly Gly Asn Ala Ile Leu
                485                 490                 495

Asn Cys Glu Val Lys Gly Asp Pro Thr Pro Thr Ile Gln Trp Asn Arg
            500                 505                 510

Lys Gly Val Asp Ile Glu Ile Ser His Arg Ile Arg Gln Leu Gly Asn
        515                 520                 525

Gly Ser Leu Ala Ile Tyr Gly Thr Val Asn Glu Asp Ala Gly Asp Tyr
    530                 535                 540

Thr Cys Val Ala Thr Asn Glu Ala Gly Val Val Glu Arg Ser Met Ser
545                 550                 555                 560

Leu Thr Leu Arg Ser Pro Pro Ile Ile Thr Leu Glu Pro Val Glu Thr
                565                 570                 575

Val Ile Asn Ala Gly Gly Lys Ile Ile Leu Asn Cys Gln Ala Thr Gly
            580                 585                 590

Glu Pro Gln Pro Thr Ile Thr Trp Ser Arg Gln Gly His Ser Ile Ser
        595                 600                 605
```

```
Trp Asp Asp Arg Val Asn Val Leu Ser Asn Asn Ser Leu Tyr Ile Ala
    610                 615                 620

Asp Ala Gln Lys Glu Asp Thr Ser Glu Phe Glu Cys Val Ala Arg Asn
625                 630                 635                 640

Leu Met Gly Ser Val Leu Val Arg Val Pro Val Ile Val Gln Val His
                645                 650                 655

Gly Gly Phe Ser Gln Trp Ser Ala Trp Arg Ala Cys Ser Val Thr Cys
            660                 665                 670

Gly Lys Gly Ile Gln Lys Arg Ser Arg Leu Cys Asn Gln Pro Leu Pro
        675                 680                 685

Ala Asn Gly Gly Lys Pro Cys Gln Gly Ser Asp Leu Glu Met Arg Asn
    690                 695                 700

Cys Gln Asn Lys Pro Cys Pro Val Asp Gly Ser Trp Ser Glu Trp Ser
705                 710                 715                 720

Leu Trp Glu Glu Cys Thr Arg Ser Cys Gly Arg Gly Asn Gln Thr Arg
                725                 730                 735

Thr Arg Thr Cys Asn Asn Pro Ser Val Gln His Gly Gly Arg Pro Cys
            740                 745                 750

Glu Gly Asn Ala Val Glu Ile Ile Met Cys Asn Ile Arg Pro Cys Pro
        755                 760                 765

Val His Gly Ala Trp Ser Ala Trp Gln Pro Trp Gly Thr Cys Ser Glu
    770                 775                 780

Ser Cys Gly Lys Gly Thr Gln Thr Arg Ala Arg Leu Cys Asn Asn Pro
785                 790                 795                 800

Pro Pro Ala Phe Gly Gly Ser Tyr Cys Asp Gly Ala Glu Thr Gln Met
                805                 810                 815

Gln Val Cys Asn Glu Arg Asn Cys Pro Ile His Gly Lys Trp Ala Thr
            820                 825                 830
```

```
Trp Ala Ser Trp Ser Ala Cys Ser Val Ser Cys Gly Gly Gly Ala Arg
        835                 840                 845

Gln Arg Thr Arg Gly Cys Ser Asp Pro Val Pro Gln Tyr Gly Gly Arg
    850                 855                 860

Lys Cys Glu Gly Ser Asp Val Gln Ser Asp Phe Cys Asn Ser Asp Pro
865                 870                 875                 880

Cys Pro Thr His Gly Asn Trp Ser Pro Trp Ser Gly Trp Gly Thr Cys
                885                 890                 895

Ser Arg Thr Cys Asn Gly Gly Gln Met Arg Arg Tyr Arg Thr Cys Asp
            900                 905                 910

Asn Pro Pro Pro Ser Asn Gly Gly Arg Ala Cys Gly Gly Pro Asp Ser
        915                 920                 925

Gln Ile Gln Arg Cys Asn Thr Asp Met Cys Pro Val Asp Gly Ser Trp
    930                 935                 940

Gly Ser Trp His Ser Trp Ser Gln Cys Ser Ala Ser Cys Gly Gly Gly
945                 950                 955                 960

Glu Lys Thr Arg Lys Arg Leu Cys Asp His Pro Val Pro Val Lys Gly
                965                 970                 975

Gly Arg Pro Cys Pro Gly Asp Thr Thr Gln Val Thr Arg Cys Asn Val
            980                 985                 990

Gln Ala Cys Pro Gly Gly Pro Gln  Arg Ala Arg Gly Ser  Val Ile Gly
        995                 1000                1005

Asn Ile  Asn Asp Val Glu Phe  Gly Ile Ala Phe Leu  Asn Ala Thr
    1010                1015                1020

Ile Thr  Asp Ser Pro Asn Ser  Asp Thr Arg Ile Ile  Arg Ala Lys
    1025                1030                1035

Ile Thr  Asn Val Pro Arg Ser  Leu Gly Ser Ala Met  Arg Lys Ile
    1040                1045                1050

Val Ser  Ile Leu Asn Pro Ile  Tyr Trp Thr Thr Ala  Lys Glu Ile
```

```
    1055                1060                1065

Gly Glu  Ala Val Asn Gly Phe  Thr Leu Thr Asn Ala  Val Phe Lys
    1070                1075                1080

Arg Glu  Thr Gln Val Glu Phe  Ala Thr Gly Glu Ile  Leu Gln Met
    1085                1090                1095

Ser His  Ile Ala Arg Gly Leu  Asp Ser Asp Gly Ser  Leu Leu Leu
    1100                1105                1110

Asp Ile  Val Val Ser Gly Tyr  Val Leu Gln Leu Gln  Ser Pro Ala
    1115                1120                1125

Glu Val  Thr Val Lys Asp Tyr  Thr Glu Asp Tyr Ile  Gln Thr Gly
    1130                1135                1140

Pro Gly  Gln Leu Tyr Ala Tyr  Ser Thr Arg Leu Phe  Thr Ile Asp
    1145                1150                1155

Gly Ile  Ser Ile Pro Tyr Thr  Trp Asn His Thr Val  Phe Tyr Asp
    1160                1165                1170

Gln Ala  Gln Gly Arg Met Pro  Phe Leu Val Glu Thr  Leu His Ala
    1175                1180                1185

Ser Ser  Val Glu Ser Asp Tyr  Asn Gln Ile Glu Glu  Thr Leu Gly
    1190                1195                1200

Phe Lys  Ile His Ala Ser Ile  Ser Lys Gly Asp Arg  Ser Asn Gln
    1205                1210                1215

Cys Pro  Ser Gly Phe Thr Leu  Asp Ser Val Gly Pro  Phe Cys Ala
    1220                1225                1230

Asp Glu  Asp Glu Cys Ala Ala  Gly Asn Pro Cys Ser  His Ser Cys
    1235                1240                1245

His Asn  Ala Met Gly Thr Tyr  Tyr Cys Ser Cys Pro  Lys Gly Leu
    1250                1255                1260

Thr Ile  Ala Ala Asp Gly Arg  Thr Cys Gln Asp Ile  Asp Glu Cys
    1265                1270                1275
```

Ala Leu Gly Arg His Thr Cys His Ala Gly Gln Asp Cys Asp Asn
1280 1285 1290

Thr Ile Gly Ser Tyr Arg Cys Val Val Arg Cys Gly Ser Gly Phe
1295 1300 1305

Arg Arg Thr Ser Asp Gly Leu Ser Cys Gln Asp Ile Asn Glu Cys
1310 1315 1320

Gln Glu Ser Ser Pro Val Thr Ser Ala Val Ser Met Pro
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